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L2	L1 same activity	64	L2
L1	retro inverso peptide	155	L1

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NEWS 22	Feb 24	PCTGEN now available on STN
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NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
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NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
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NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 45	Jun 25	HSDB has been reloaded

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=> s retro inverso peptide
L1           96 RETRO INVERSO PEPTIDE

=> s l1 and review/dt
L2            0 L1 AND REVIEW/DT

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L3           79 L1 AND PY<2001

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L4   ANSWER 1 OF 52  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   2001:230910  BIOSIS
DN   PREV200100230910
TI   Probing SAR of FLRF-NH2 with its N- and C-terminally modified analogs and
     retro-inverso peptides.
AU   Kubiak, Teresa M. (1); Larsen, Martha J. (1); Dutton, Fred E. (1);
     Friedman, Alan R. (1)
CS   (1) Animal Health Discovery Research, Pharmacia and Upjohn, Kalamazoo, MI,
     49001 USA
SO   Fields, Gregg B.; Tam, James P.; Barany, George. (2000) pp. 762-763.
     Peptides for the new millennium. print.
     Publisher: Kluwer Academic Publishers 3300 AA, Dordrecht, Netherlands.
     Meeting Info.: 16th American Peptide Symposium Minneapolis, MI, USA June
     26-July 01, 1999
```

ISBN: 0-7923-6445-7 (cloth).
DT Book; Conference
LA English
SL English

L4 ANSWER 2 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:417340 BIOSIS
DN PREV200000417340
TI Solid-phase synthesis of partially-modified retro and retro-inverso psi(NHCH(CF3))-peptides.
AU Volonterio, Alessandro (1); Bravo, Pierfrancesco; Moussier, Nathalie; Zanda, Matteo (1)
CS (1) Dipartimento di Chimica del Politecnico, Via Mancinelli 7, I-20131, Milano Italy
SO Tetrahedron Letters, (**12 August, 2000**) Vol. 41, No. 33, pp. 6517-6521. print.
ISSN: 0040-4039.
DT Article
LA English
SL English
AB The solid-phase synthesis of a novel class of retro and **retro-inverso peptides** featuring a psi(NHCH(CF3)) surrogate of the classical (NH-CO) retro-peptide bond has been accomplished. Wang resin bound alpha-amino esters 2 were engaged in Michael-type N-additions with 3-(E-enoyl)-1,3-oxazolidin-2-one 3, which took place very effectively. Highly chemoselective exocyclic oxazolidinone cleavage, followed by parallel couplings of the resulting polymer bound pseudo-peptides 6 with further alpha-amino esters, and final release from the resins 7 delivered a library of nine psi(NHCH(CF3)) retro and retro-inverso pseudo-tripeptides 8 with purity ranging from 75 to > 95%.

L4 ANSWER 3 OF 52 MEDLINE DUPLICATE 1
AN 2000483575 MEDLINE
DN 20457139 PubMed ID: 11000007
TI Design and solution structure of functional peptide mimetics of nerve growth factor.
AU Beglova N; Maliartchouk S; Ekiel I; Zaccaro M C; Saragovi H U; Gehring K
CS Department of Biochemistry and Montreal Joint Centre for Structural Biology, McGill University, 3655 Promenade Sir William Osler, Montreal, Quebec H3G 1Y6, Canada.
SO JOURNAL OF MEDICINAL CHEMISTRY, (**2000 Sep 21**) 43 (19) 3530-40.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001012
AB The C-D loop in nerve growth factor (NGF) is involved in binding to the NGF receptor, TrkA. It is flexible and adopts several different types conformations in different NGF crystal forms. We have previously shown that a small cyclic peptide derived from the C-D loop of NGF binds to the TrkA receptor by mimicking the structure of this loop. To understand structure-function relationships in NGF C-D loop mimetics, we have produced a series of peptides predicted to form different types of beta-turns. The peptides were tested for their ability to promote cell survival in serum-free medium and to induce TrkA tyrosine phosphorylation. NMR structural studies were used to determined the backbone conformation and the spatial orientation of side chains involved in binding to the TrkA receptor. Peptides that form type I or type gammaL-alphaR beta-turns were the most active. The variety of active loop conformations suggests that the mimetics (and NGF) accommodate the binding site on TrkA by an 'induced

fit' mechanism. In agreement with this hypothesis, NMR relaxation measurements detected both fast and slow motion in the peptides. We also characterized a **retro-inverso peptide** derived from the NGF C-D loop. This D-amino acid cyclic peptide did not adopt a conformation homologous to the NGF C-D loop and was inactive. This may be representative of difficulties in producing structural and functional mimetics by retro-inverso schemes.

L4 ANSWER 4 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:78061 BIOSIS
DN PREV200100078061
TI A stable prosaposin **retro-inverso peptide** exacerbates ischemia-induced behavioral deficits in rabbits: comparison with the neuroprotective neurosteroid dehydroepiandrosterone sulfate.
AU Chapman, D. F. (1); Araujo, D. M.; Zivin, J. A.; Lapchak, P. A.
CS (1) UCSD, La Jolla, CA USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-287.5. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English
AB Evidence suggests that prosaposin and neurosteroids can rescue neurons from ischemic damage and excitoxicity. Because of their potential neuroprotective properties, both RIP and DHEAS may be useful in treating ischemic stroke. We examined the behavioral effects of a stable 11-mer RIP also known as Prosaptide (all D amino acids: LLEETANNDLL) and DHEAS in rabbits exposed to reversible spinal cord ischemia produced by temporary occlusion of the infrarenal aorta; RIP (1 mg/kg) or DHEAS (50 mg/kg) were administered IV 5 minutes following various durations of aortic occlusion ranging from 15 to 60 min, which allows for the calculation of the duration (min) associated with a 50% probability of permanent paraplegia (P50) for each experimental group. A drug was considered to be neuroprotective only if it prolonged the P50 compared to the vehicle-treated control group, which was approximately 25-28 min. Treatment with RIP significantly ($p<0.05$) decreased the P50 to 20 min (20% reduction), whereas DHEAS significantly ($p<0.05$) prolonged the P50 to 38 min (35% increase). The prominent neuroprotective effects that were observed with DHEAS included increased mobility, tactile sensation and hind limb use. In contrast, RIP exacerbated ischemia-induced behavioral deficits and increased paraplegia. Overall, our study shows that although neurotrophic-like properties have been documented for both RIP and DHEAS, only the latter promotes recovery of spinal cord neuron function following ischemia, suggesting that it may have therapeutic benefits for the treatment of ischemic stroke.

L4 ANSWER 5 OF 52 MEDLINE DUPLICATE 2
AN 1999121111 MEDLINE
DN 99121111 PubMed ID: 9920919
TI Solution structure of a **retro-inverso peptide** analogue mimicking the foot-and-mouth disease virus major antigenic site. Structural basis for its antigenic cross-reactivity with the parent peptide.
AU Petit M C; Benkirane N; Guichard G; Du A P; Marraud M; Cung M T; Briand J P; Muller S
CS Laboratoire de Chimie-Physique Macromoleculaire, UMR 7568 CNRS, ENSIC-INPL, 54000 Nancy, France.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1999 Feb 5)** 274 (6) 3686-92.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
OS PDB-1BCV; PDB-1BFW
EM 199902
ED Entered STN: 19990316
Last Updated on STN: 20000303
Entered Medline: 19990226
AB The antigenic activity of a 19-mer peptide corresponding to the major antigenic region of foot-and-mouth disease virus and its retro-enantiomeric analogue was found to be completely abolished when they were tested in a biosensor system in trifluoroethanol. This suggests that the folding pattern, which is alpha-helix in trifluoroethanol (confirmed by CD measurement), does not correspond to the biologically relevant conformation(s) recognized by antibodies. The NMR structures of both peptides were thus determined in aqueous solution. These studies showed that the two peptides exhibit similar folding features, particularly in their C termini. This may explain in part the cross-reactive properties of the two peptides in aqueous solution. However, the retro-inverso analogue appears to be more rigid than the parent peptide and contains five atypical beta-turns. This feature may explain why retro-inverso foot-and-mouth disease virus peptides are often better recognized than the parent peptide by anti-virion antibodies.

L4 ANSWER 6 OF 52 MEDLINE DUPLICATE 3
AN 1999388009 MEDLINE
DN 99388009 PubMed ID: 10458771
TI Inhibition of experimental autoimmune encephalomyelitis in SJL mice by oral administration of retro-inverso derivative of encephalitogenic epitope P87-99.
AU Marino M; Ippolito A; Fassina G
CS Biopharmaceuticals, TECNOGEN S.C.p.A., Science Park, Piana di Monte Verna, Italy.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1999 Aug)** 29 (8) 2560-6.
Journal code: 1273201. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990914
AB Retro-inverso modification of peptides preserves parent peptide overall topology and provides at the same time stability to proteolysis, leading to derivatives with prolonged half-life in vitro and in vivo. In this study the encephalitogenic epitope P87 - 99 of myelin basic protein has been prepared in the retro-inverso form to examine its biological activity in a murine model of multiple sclerosis. Experiments of in vivo T cell tolerance induction in SJL mice revealed that the **retro-inverso peptide** was able to induce a selective T cell hyporesponsiveness, as measured by a reduction in the proliferative response of lymphnode T cells after antigen challenge. Oral administration of **retro-inverso peptide** decreased the disease severity significantly and delayed considerably the disease onset in treated mice. Enhancement of resistance to proteolysis by retro-inverso modification of encephalitogenic epitopes may increase the therapeutic value of oral tolerance induction in the treatment of multiple sclerosis and other Th1-associated inflammatory disorders.

L4 ANSWER 7 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:281588 BIOSIS
DN PREV199800281588
TI The potential of **retro-inverso peptides** as synthetic vaccines.
AU Van Regenmortel, M. H. V. (1); Guichard, G.; Benkirane, N.; Briand, J.-P.;

Muller, S.; Brown, F.
CS (1) Inst. Biol. Mol. et Cell., CNRS UPR 9021, 15 rue Rene Descartes, F-67084 Strasbourg Cedex France
SO Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 139-143. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens. Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization
. ISSN: 0301-5149. ISBN: 3-8055-6640-9.
DT Book; Conference
LA English

L4 ANSWER 8 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:16628 BIOSIS
DN PREV199900016628
TI A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a retro-inverso delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons.
AU Aldrian-Herrada, Gudrun; Desarmenien, Michel G.; Orcel, Helene; Boissin-Agasse, Line; Mery, Jean; Brugidou, Jean; Rabie, Alain (1)
CS (1) CNRS-UPR 9055, Biologie Neurones Endocrines, CCIPE, 141 rue Cardonille, 34094 Montpellier Cedex 5 France
SO Nucleic Acids Research, (**Nov. 1, 1998**) Vol. 26, No. 21, pp. 4910-4916.
ISSN: 0305-1048.
DT Article
LA English
AB A peptide nucleic acid (PNA) antisense for the AUG translation initiation region of prepro-oxytocin mRNA was synthesized and coupled to a **retro-inverso peptide** that is rapidly taken up by cells. This bioconjugate was internalized by cultured cerebral cortex neurons within minutes, according to the specific property of the vector peptide. The PNA alone also entered the cells, but more slowly. Cell viability was unaffected when the PNA concentrations were lower than 10 muM and incubation times less than for 24 h. Magnocellular neurons from the hypothalamic supraoptic nucleus, which produce oxytocin and vasopressin, were cultured in chemically defined medium. Both PNA and vector peptide-PNA depressed the amounts of the mRNA coding for prepro-oxytocin in these neurons. A scrambled PNA had no effect and the very cognate prepro-vasopressin mRNA was not affected. The antisense PNA also depressed the immunocytochemical signal for prepro-oxytocin in this culture in a dose- and time-dependent manner. These results show that PNAs driven by the retro-inverso vector peptide are powerful antisense reagents for use on cells in culture.

L4 ANSWER 9 OF 52 MEDLINE
AN 1999097766 MEDLINE
DN 99097766 PubMed ID: 9881091
TI A 'retro-inverso' PNA: structural implications for DNA and RNA binding.
AU Krotz A H; Larsen S; Buchardt O; Eriksson M; Nielsen P E
CS Center for Biomolecular Recognition, H. C. Orsted Institute, University of Copenhagen, Denmark.
SO BIOORGANIC AND MEDICINAL CHEMISTRY, **(1998 Nov)** 6 (11) 1983-92.
Journal code: 9413298. ISSN: 0968-0896.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990216
Last Updated on STN: 19990216

Entered Medline: 19990202

AB 'Retro-inverso' peptide nucleic acid (PNA) monomers of thymine (T*: N-(amidomethyl)-N-(N1-thyminyl-acetyl)-beta-alanyl) (and adenine) have been prepared and introduced in PNA oligomers. A homo 'retro-inverso' T*8 PNA was found not to hybridize to a complementary DNA or RNA oligonucleotide, whereas introduction of one retro-inverso thymine unit into the middle of a normal PNA 15-mer resulted in a c.a. 8 degrees C destabilization of the complex of this oligomer with a complementary DNA or RNA oligomer. In an effort to compensate for the structural nucleobase 'phase-shift' caused by the T* monomer by also introducing a beta-alanine monomer it is concluded that the effect of the T* backbone is -7 degrees C when hybridizing to DNA and -4.5 degrees C when hybridizing to RNA. Nonetheless, the T* unit shows good sequence discrimination comparable to that of normal PNA. Molecular dynamics simulations indicate an unfavourable conformation of the backbone amide carbonyl group resulting in reduced interaction with the aqueous medium and an 'electrostatic clash' with the carbonyl of the nucleobase linker. These results show that a simple inversion of an amide bond in the PNA backbone has a dramatic, and hardly predictable, effect on the DNA mimicking properties of the oligomer.

L4 ANSWER 10 OF 52 MEDLINE
AN 1998214886 MEDLINE
DN 98214886 PubMed ID: 9554267
TI The potential of **retro-inverso peptides** as synthetic vaccines.
AU Van Regenmortel M H; Guichard G; Benkirane N; Briand J P; Muller S; Brown F
CS Institut de Biologie Moleculaire et Cellulaire, CNRS UPR, Strasbourg, France.
SO DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, **(1998)** 92 139-43.
Journal code: 0427140. ISSN: 0301-5149.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980708
Last Updated on STN: 20021218
Entered Medline: 19980625
AB Retro-inverso (RI) peptides, also called all-D-retro peptides, have been shown to mimic the antigenic and immunogenic properties of L-peptides successfully. RI peptides corresponding to the loop 141-159 of the VP1 protein of foot-and-mouth disease virus (FMDV) have been synthesized and used to immunize rabbits and guinea pigs. These peptides induced longer-lasting and higher antibody titres in immunized animals than did the corresponding L-peptides and the antibodies cross-reacted strongly with virus particles and with L-peptides. Antisera raised to RI peptides had in vitro virus neutralization titres equal to or better than those obtained after immunization with classical FMDV antigens and L-peptides. In view of their increased stability, RI peptides may overcome some of the shortcomings of synthetic viral vaccines based on L-peptides.

=> d 11-20 bib ab

L4 ANSWER 11 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:414053 BIOSIS
DN PREV199800414053
TI On the potential of **retro-inverso peptides** in vaccine design.
AU Muller, S. (1); Briand, J. P.
CS (1) Inst. Biologie Moleculaire Cellulaire, UPR 9021 CNRS, 15 rue Descartes, F-67000 Strasbourg France

SO Research in Immunology, (**Jan., 1998**) Vol. 149, No. 1, pp. 55-57.
Meeting Info.: Euroconference on New Trends in Vaccine Research and Development: Adjuvants, Delivery Systems and Antigen Formulations Paris, France February 26-28, 1998
ISSN: 0923-2494.
DT Conference
LA English

L4 ANSWER 12 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:465325 BIOSIS
DN PREV199799764528
TI Immunochemical recognition of **retro-inverso peptides** and their potential as synthetic vaccines.
AU Van Regenmortel, Marc H. V.
CS CNRS UPR 9021, Inst. Biologie Moleculaire Cellulaire, F-67084 Strasbourg Cedex France
SO Brown, F. [Editor]; Burton, D. [Editor]; Doherty, P. [Editor]; Mekalanos, J. [Editor]. Vaccines (Cold Spring Harbor), (1997) Vol. 97, pp. 9-15.
Vaccines (Cold Spring Harbor); Molecular approaches to the control of infectious diseases.
Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive, Plainview, New York 11803, USA.
Meeting Info.: Fourteenth Annual Meeting on Modern Approaches to the Control of Infectious Diseases Cold Spring Harbor, New York, USA September 9-13, 1996
ISSN: 0899-4056. ISBN: 0-87969-516-1.
DT Book; Conference
LA English

L4 ANSWER 13 OF 52 MEDLINE DUPLICATE 4
AN 1998024168 MEDLINE
DN 98024168 PubMed ID: 9356486
TI A **retro-inverso peptide** corresponding to the GH loop of foot-and-mouth disease virus elicits high levels of long-lasting protective neutralizing antibodies.
AU Briand J P; Benkirane N; Guichard G; Newman J F; Van Regenmortel M H; Brown F; Muller S
CS Institut de Biologie Moleculaire et Cellulaire, Unite Propre de Recherche 9021, Centre National de la Recherche Scientifique, Strasbourg, France.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1997 Nov 11)** 94 (23) 12545-50.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971216
AB Peptides corresponding to the immunodominant loop located at residues 135-158 on capsid protein VP1 of foot-and-mouth disease virus (FMDV) generally elicit high levels of anti-peptide and virus-neutralizing antibodies. In some instances, however, the level of neutralizing antibodies is low or even negligible, even though the level of anti-peptide antibodies is high. We have shown previously that the antigenic activity of peptide 141-159 of VP1 of a variant of serotype A can be mimicked by a retro-inverso (all-D retro or retroenantio) peptide analogue. This retro-inverso analogue induced greater and longer-lasting antibody titers than did the corresponding L-peptide. We now show that a single inoculation of the retro-inverso analogue elicits high levels of neutralizing antibodies that persist longer than those induced against the corresponding L-peptide and confer substantial protection in guinea pigs challenged with the cognate virus. In view of the high stability to

proteases of **retro-inverso peptide** analogues
and their enhanced immunogenicity, these results have practical relevance in designing potential peptide vaccines.

L4 ANSWER 14 OF 52 MEDLINE DUPLICATE 5
AN 97249852 MEDLINE
DN 97249852 PubMed ID: 9095678
TI Structural comparison between retro-inverso and parent peptides: molecular basis for the biological activity of a retro-inverso analogue of the immunodominant fragment of VP1 coat protein from foot-and-mouth disease virus.
AU Carver J A; Esposito G; Viglino P; Fogolari F; Guichard G; Briand J P; Van Regenmortel M H; Brown F; Mascagni P
CS Dipartimento di Scienze e Tecnologie Biomediche Universita di Udine, Italy.
SO BIOPOLYMERS, **(1997 Apr 15)** 41 (5) 569-90.
Journal code: 0372525. ISSN: 0006-3525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970602
Last Updated on STN: 20021218
Entered Medline: 19970521
AB Antibodies induced against intact foot-and-mouth disease Virus (FMDV) particles bind to the retro-inverso analogue of fragment 141-159 of the viral coat protein VP1 of FMDV, variant A, equally well as to the parent peptide. A conformational investigation of this **retro-inverso peptide** was carried out by nmr spectroscopy and restrained molecular modeling in order to identify the structural basis for the antigenic mimicry between these retro-inverso and parent peptides. In 100% trifluoroethanol a well-defined left-handed alpha-helical region exists from residue 150 to residue 159, which is consistently present in all conformational families obtained from restrained modelling. A less-defined left-handed helical region is present in the tract 144-148, which is also consistent for all structures. Conformational flexibility exists about Gly149, which leads to two types of structures, either bent or linear. In the bent structures, a three-residue inverse tight turn is found, which can be classified as an inverse gamma-turn centered at Gly149. The overall structural features of the **retro-inverso peptide** are shown to be similar to those of the parent L-peptide. The two molecules, however, are roughly mirror images because they share inherently chiral secondary structure elements. By comparing these conformational conclusions with the x-ray structure of the Fab complex of a corresponding VP1 antigenic fragment, a rationale is proposed to account for the topological requirements of specific recognition that are implied by the equivalent antigenic activity of the natural and retro-inverso compounds.

L4 ANSWER 15 OF 52 MEDLINE DUPLICATE 6
AN 97295648 MEDLINE
DN 97295648 PubMed ID: 9151257
TI Synthesis and activity of partial retro-inverso analogs of the antimetastatic laminin-derived peptide, YIGSR-NH2.
AU Zhao M; Kleinman H K; Mokotoff M
CS Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pennsylvania, USA.
NC RR04664-01 (NCRR)
SO JOURNAL OF PEPTIDE RESEARCH, **(1997 Mar)** 49 (3) 240-53.
Journal code: 9707067. ISSN: 1397-002X.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199707
ED Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970724
AB This paper describes the synthesis and biological evaluation of six partial retro-inverso peptidomimetic analogs of YIGSR-NH2, a synthetic peptide from the beta 1 chain of laminin, which has antimetastatic activity. The intent was to improve the antimetastatic potency of YIGSR-NH2 by limiting the in vivo enzymatic degradation through the incorporation of fraudulent peptide bonds. We have prepared the following **retro-inverso peptides**, Tyr-Ile-Gly-Ser-gArg-CHO (1), Tyr-gIle-mGly-Ser-Arg-NH2 (2), Tyr-gIle-mGly-Ser-gArg-CHO (3), gTyr-D-rIle-mGly-Ser-Arg-NH2 (4), Tyr-Ile-Gly-gSer-D-rArg-CHO (5) and Tyr-gIle-rGly-D-rSer-D-rArg-CHO (6). In vitro assays for B16F10 melanoma cell adhesion showed no significant activity for these six peptides. Peptides 1-3, 5 and 6 were further tested, in vivo, for their ability to inhibit tumor metastases to the lung in mice injected in the tail vein with B16F10 melanoma cells. All five of the **retro-inverso peptides** tested showed statistically significant inhibition of metastasis, but the most active peptides were 5 and 6, which showed 57 and 69% inhibition of metastasis, respectively.

L4 ANSWER 16 OF 52 MEDLINE DUPLICATE 7
AN 97332614 MEDLINE
DN 97332614 PubMed ID: 9188848
TI On the immunogenic properties of **retro-inverso peptides**. Total retro-inversion of T-cell epitopes causes a loss of binding to MHC II molecules.
AU Herve M; Maillere B; Mourier G; Texier C; Leroy S; Menez A
CS CEA, Departement d'Ingenierie et d'Etudes des Proteines, CE Saclay, Gif-sur-Yvette, France.
SO MOLECULAR IMMUNOLOGY, **(1997 Feb)** 34 (2) 157-63.
Journal code: 7905289. ISSN: 0161-5890.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707
ED Entered STN: 19970721
Last Updated on STN: 19970721
Entered Medline: 19970708
AB Retro-inversion is considered an attractive approach for drug and vaccine design since it provides the modified peptides with higher resistance to proteolytic degradation. We therefore investigated in detail the effect of retro-inversion on the immunological properties of synthetic peptides. We have synthesized retro-inverso analogues of MHC II restricted peptides that thus contained the correct orientation of the side chains but an inverse main chain. Retro-inversion made the peptides unable to compete in I E(d) or I A(d) binding tests, demonstrating a very low, if any, capacity to bind to MHC II molecules. These results confirm previous structural data that hydrogen bonds between residues of MHC II molecules and the main chain of antigenic peptides play a major interacting role. In vito experiments further showed that retro-inversion of a T-cell epitope causes its inability to either sustain in vitro T-cell stimulation or to prime specific T cells. Moreover, the **retro-inverso peptide** was not recognized by antibodies raised against the native peptide and did not elicit antibodies when injected into BALB/c mice. **Retro-inverso peptides** appear to be poor immunogens as a result of their weak capacity to bind to MHC II molecules. As an advantage, they are not expected to trigger undesirable humoral responses such as hypersensitivity or allergic disease. These results also provide a molecular explanation regarding the weak immunogenicity of D-amino acids containing polypeptides.

L4 ANSWER 17 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:175210 BIOSIS
DN PREV199799466923
TI Small **retro-inverso peptides** recognize MHC class II HLA, DR(alpha, beta-1*0401.
AU Howard, Susan C. (1); Zacheis, Michelle L.; Bono, Christine P.; Welply, Joseph K.; Hanson, Gunnar J.; Vuletich, Jennifer L.; Bedell, Louis J.; Summers, Neena L.; Schwartz, Benjamin D.; Woulfe, Susan L.
CS (1) G.D. Searle Dep. Immunol., St. Louis, MO 63198 USA
SO Protein and Peptide Letters, (1997) Vol. 4, No. 1, pp. 63-68.
ISSN: 0929-8665.
DT Article
LA English
AB We have synthesized a series of retro-inverso D-peptide analogues and a peptoid analog that mimic potent seven residue L-peptide ligands for DR(alpha, beta-1*0401). The L-peptide ligands compete against binding of a 13 residue biotinylated ligand, HA307-319 (IC-50 60nM), with competing peptide IC-50 S ranging from 30-200nm. The highest affinity heptamer retro-inverso D-peptide tested gave IC-50 10-mu-M. No binding of the peptoid analog was detected.

L4 ANSWER 18 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1996:454003 BIOSIS
DN PREV199699176359
TI Mimicry of viral epitopes with **retro-inverso peptides** of increased stability.
AU Benkirane, N. (1); Guichard, G.; Briand, J. P.; Muller, S.; Brown, F.; Van Regenmortel, M. H. V.
CS (1) Inst. Biol. Mol. Cell., CNRS, 15 rue Descartes, F-67084 Strasbourg France
SO Brown, F. [Editor]. Developments in Biological Standardization, (1996) Vol. 87, pp. 283-291. Developments in Biological Standardization; New approaches to stabilisation of vaccines potency.
Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Geneva, Switzerland May 29-31, 1995
ISSN: 0301-5149. ISBN: 3-8055-6309-4.
DT Book; Conference
LA English

L4 ANSWER 19 OF 52 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:24961 BIOSIS
DN PREV199799324164
TI Synthesis and biological properties of partially modified retro and retro-inverso pseudo peptides of Arg-Gly-Asp (RGD.
AU Nishikawa, Naoyuki (1); Komazawa, Hiroyuki; Orikasa, Atsushi; Yoshikane, Mitsuo; Yamaguchi, Jiro; Kojima, Masayoshi; Ono, Mitsunori; Itoh, Isamu; Azuma, Ichiro; Fujii, Hideki; Murata, Jun; Saiki, Ikuo
CS (1) Ashigara Res. Lab., Fuji Photo Film Co. Ltd., Minamiashigara, Kanagawa 250-01 Japan
SO Bioorganic & Medicinal Chemistry Letters, (1996) Vol. 6, No. 22, pp. 2725-2728.
ISSN: 0960-894X.
DT Article
LA English
AB Partially modified retro and **retro-inverso peptide** analogs of Arg-Gly-Asp (RGD) were synthesized and examined their inhibitory effects on experimental lung metastasis of murine melanoma and adenosine 5'-diphosphate (ADP) induced platelet aggregation. The analogs showed efficient therapeutic potency for the tumor metastasis but low inhibitory effect on ADP induced platelet aggregation.

L4 ANSWER 20 OF 52 MEDLINE DUPLICATE 8

AN 97020448 MEDLINE
DN 97020448 PubMed ID: 8866827
TI Inhibition of angiotensin converting enzyme and potentiation of bradykinin by retro-inverso analogues of short peptides and sequences related to angiotensin I and bradykinin.
AU Carmona A K; Juliano L
CS Department of Biophysics, Escola Paulista de Medicina, Sao Paulo, Brazil.
SO BIOCHEMICAL PHARMACOLOGY, **(1996 Apr 26)** 51 (8) 1051-60.
Journal code: 0101032. ISSN: 0006-2952.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961127
AB There is pharmacological evidence indicating that, in addition to the inhibition of angiotensin converting enzyme (ACE; EC 3.4.15.1), the potentiation of bradykinin (BK) responses may also involve the BK receptor or some binding site in the structures involved in the contractile response to this peptide. Dipeptides such as Val-Trp and some of its analogues as well as tripeptide homologues, including total and partial **retro-inverso peptides**, were synthesized and assayed for their ability to inhibit purified guinea pig plasma ACE and to potentiate the action of BK on the isolated ileum of the same species. The peptides containing the P2-P1, P1-P'1, and P'1-P'2 inverted amide bonds inhibited ACE, were resistant to hydrolysis, and, depending on the amino acid composition, some of them potentiated the contractile response to BK while others did not. Des-[Arg1]-BK, which has an intrinsic activity at concentrations higher than 10(-5) M, and the very dissimilar angiotensin I (AI) analogue [Cys5-Cys10]-angiotensin-I-(5-10)-amide, which has no detectable contractile activity, were able to inhibit ACE and potentiate BK. In contrast to these peptides, BPP5a and BPP9a from Bothrops jararaca venom, and Potentiators B and C from Agkistrodon halys blomhoffi venom were more effective as BK potentiators than as ACE inhibitors. In conclusion, we have synthesized and assayed compounds that preferentially inhibit ACE, e.g. retro-inverso tripeptides, or potentiate the response of smooth muscle to BK, e.g. snake venom peptides.

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NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
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NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 45	Jun 25	HSDB has been reloaded

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L1          278 RETRO INVERSO

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L2          222 L1 AND PEPTIDE

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L3          187 L2 AND PY<2001

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L4   ANSWER 1 OF 115  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   2001:230910  BIOSIS
DN   PREV200100230910
TI   Probing SAR of FLRF-NH2 with its N- and C-terminally modified analogs and
     retro-inverso peptides.
AU   Kubiak, Teresa M. (1); Larsen, Martha J. (1); Dutton, Fred E. (1);
     Friedman, Alan R. (1)
CS   (1) Animal Health Discovery Research, Pharmacia and Upjohn, Kalamazoo, MI,
     49001 USA
SO   Fields, Gregg B.; Tam, James P.; Barany, George. (2000) pp. 762-763.
     Peptides for the new millennium. print.
     Publisher: Kluwer Academic Publishers 3300 AA, Dordrecht, Netherlands.
     Meeting Info.: 16th American Peptide Symposium Minneapolis, MI, USA June
     26-July 01, 1999
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ISBN: 0-7923-6445-7 (cloth).
DT Book; Conference
LA English
SL English

L4 ANSWER 2 OF 115 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:417340 BIOSIS
DN PREV200000417340
TI Solid-phase synthesis of partially-modified retro and **retro-inverso** psi(NHCH(CF3))-**peptides**.
AU Volonterio, Alessandro (1); Bravo, Pierfrancesco; Moussier, Nathalie; Zanda, Matteo (1)
CS (1) Dipartimento di Chimica del Politecnico, Via Mancinelli 7, I-20131, Milano Italy
SO Tetrahedron Letters, (**12 August, 2000**) Vol. 41, No. 33, pp. 6517-6521. print.
ISSN: 0040-4039.
DT Article
LA English
SL English
AB The solid-phase synthesis of a novel class of retro and **retro-inverso peptides** featuring a psi(NHCH(CF3)) surrogate of the classical (NH-CO) retro-**peptide** bond has been accomplished. Wang resin bound alpha-amino esters 2 were engaged in Michael-type N-additions with 3-(E-enoyl)-1,3-oxazolidin-2-one 3, which took place very effectively. Highly chemoselective exocyclic oxazolidinone cleavage, followed by parallel couplings of the resulting polymer bound pseudo-**peptides** 6 with further alpha-amino esters, and final release from the resins 7 delivered a library of nine psi(NHCH(CF3)) retro and **retro-inverso** pseudo-tripeptides 8 with purity ranging from 75 to > 95%.

L4 ANSWER 3 OF 115 MEDLINE DUPLICATE 1
AN 2000483575 MEDLINE
DN 20457139 PubMed ID: 11000007
TI Design and solution structure of functional **peptide** mimetics of nerve growth factor.
AU Beglova N; Maliartchouk S; Ekiel I; Zaccaro M C; Saragovi H U; Gehring K
CS Department of Biochemistry and Montreal Joint Centre for Structural Biology, McGill University, 3655 Promenade Sir William Osler, Montreal, Quebec H3G 1Y6, Canada.
SO JOURNAL OF MEDICINAL CHEMISTRY, (**2000 Sep 21**) 43 (19) 3530-40.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001012
AB The C-D loop in nerve growth factor (NGF) is involved in binding to the NGF receptor, TrkA. It is flexible and adopts several different types conformations in different NGF crystal forms. We have previously shown that a small cyclic **peptide** derived from the C-D loop of NGF binds to the TrkA receptor by mimicking the structure of this loop. To understand structure-function relationships in NGF C-D loop mimetics, we have produced a series of **peptides** predicted to form different types of beta-turns. The **peptides** were tested for their ability to promote cell survival in serum-free medium and to induce TrkA tyrosine phosphorylation. NMR structural studies were used to determined the backbone conformation and the spatial orientation of side chains involved in binding to the TrkA receptor. **Peptides** that form type I or type gammaL-alphaR beta-turns were the most active. The variety of active

loop conformations suggests that the mimetics (and NGF) accommodate the binding site on TrkA by an 'induced fit' mechanism. In agreement with this hypothesis, NMR relaxation measurements detected both fast and slow motion in the **peptides**. We also characterized a **retro -inverso peptide** derived from the NGF C-D loop. This D-amino acid cyclic **peptide** did not adopt a conformation homologous to the NGF C-D loop and was inactive. This may be representative of difficulties in producing structural and functional mimetics by **retro-inverso** schemes.

L4 ANSWER 4 OF 115 MEDLINE
AN 2000437793 MEDLINE
DN 20405631 PubMed ID: 10946275
TI Binding kinetics, structure-activity relationship, and biotransformation of the complement inhibitor compstatin.
AU Sahu A; Soulika A M; Morikis D; Spruce L; Moore W T; Lambris J D
CS Protein Chemistry Laboratory, Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA.
NC AI 30040 (NIAID)
CA 16520 (NCI)
GM 56698 (NIGMS)
+
SO JOURNAL OF IMMUNOLOGY, **(2000 Sep 1)** 165 (5) 2491-9.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000919
AB We have previously identified a 13-residue cyclic **peptide**, Compstatin, that binds to complement component C3 and inhibits complement activation. Herein, we describe the binding kinetics, structure-activity relationship, and biotransformation of Compstatin. Biomolecular interaction analysis using surface-plasmon resonance showed that Compstatin bound to native C3 and its fragments C3b and C3c, but not C3d. While binding of Compstatin to native C3 was biphasic, binding to C3b and C3c followed the 1:1 Langmuir binding model; the affinities of Compstatin for C3b and C3c were 22- and 74-fold lower, respectively, than that of native C3. Analysis of Compstatin analogs synthesized for structure-function studies indicated that 1) the 11-membered ring between disulfide-linked Cys2-Cys12 constitutes a minimal structure required for optimal activity; 2) **retro-inverso** isomerization results in loss of inhibitory activity; and 3) some residues of the type I beta-turn segment also interact with C3. In vitro studies of Compstatin in human blood indicated that a major pathway of biotransformation was the removal of Ile1, which could be blocked by N-acetylation of the **peptide**. These findings indicate that acetylated Compstatin is stable against enzymatic degradation and that the type I beta-turn segment is not only critical for preservation of the conformational stability, but also involved in intermolecular recognition.

L4 ANSWER 5 OF 115 MEDLINE
AN 2000273399 MEDLINE
DN 20273399 PubMed ID: 10815952
TI Determination of biophysical parameters of polypeptide **retro-inverso** isomers and their analogues by capillary electrophoresis.
AU Hearn M T; Keah H H; Boysen R I; Messana I; Misiti F; Rossetti D V; Giardina B; Castagnola M
CS Department of Biochemistry and Molecular Biology, Monash University, Clayton, Australia.. milton.hearn@med.monash.edu.au
SO ANALYTICAL CHEMISTRY, **(2000 May 1)** 72 (9) 1964-72.

Journal code: 0370536. ISSN: 0003-2700.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 20000629
Last Updated on STN: 20000629
Entered Medline: 20000621
AB The relationship between the electrophoretic mobility, microobs, Stokes radius, rs, ionization state, and solution conformation of the all L-alpha-polypeptide, 1, the corresponding retro-all D-alpha-polypeptide, 2, and several truncated analogues, 3-5, has been investigated under low pH buffer conditions by high-performance capillary zonal electrophoresis (HPCZE) with coated capillaries. The results confirm that, under these conditions, the all L-alpha-polypeptide, 1, and its **retro-inverso** isomer, 2, exhibit nonidentical electrophoretic mobilities and thus different Stokes radii. At higher pH values, i.e., pH 5.0, the electrophoretic behavior of this **retro-inverso** isomer pair, however, converges. These results indicate that variations in the dipole characteristics of the polypeptide main chain and subtle differences introduced by the spatial constraints of the L-alpha-Pro-->D-alpha-Pro residue replacement lead to differences in the Stokes radii and electrophoretic mobilities of these polypeptides. Since the observed electrophoretic mobilities, microobs, reflect the mean of the mobilities of each charge species participating according to their Stokes radius or their intrinsic charge and mole fraction abundances, the results confirm that polypeptide **retro-inverso** isomers with unmodified amino and carboxy termini are resolvable. This outcome was achieved despite their notional topographical and conformational similarities as assessed from high-field proton nuclear magnetic resonance (1H NMR) spectroscopy and circular dichroism (CD) spectroscopy.

L4 ANSWER 6 OF 115 MEDLINE DUPLICATE 2
AN 2000139754 MEDLINE
DN 20139754 PubMed ID: 10673395
TI Structure-function analysis of the 7B2 CT **peptide**.
AU Apletalina E V; Juliano M A; Juliano L; Lindberg I
CS Department of Biochemistry, Louisiana State University Health Sciences Center, New Orleans, Louisiana, 70112, USA.
NC K02 DA00204 (NIDA)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(2000 Jan 27)** 267 (3) 940-2.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000320
Last Updated on STN: 20021026
Entered Medline: 20000309
AB Prohormone convertases play important roles in the proteolytic conversion of many protein precursors. The neuroendocrine protein 7B2 and its 31-residue carboxyl-terminal (CT) **peptide** potently and specifically inhibit prohormone convertase 2 (PC2). We have analyzed the residues contributing to inhibition using N-terminal truncation and alanine scanning. Removal of more than 3 residues from the amino-terminal end of CT1-18 resulted in a more than 190-fold drop in inhibitory activity, showing that most of the residues between 3 and 18 are required for inhibition. In agreement, an Ala scan indicated that only 4 residues could be replaced with Ala without losing mid-nanomolar inhibitory potency; in particular, Gln7, Gln9, and Asp12 could be Ala-substituted to yield **peptides** with a similar inhibitory potency to the starting

peptide. The all-d-**retro-inverso**, all-l-inverso, and all-d analogues of CT **peptide** were completely inactive, indicating that amino acid side chains and the CT **peptide** main chain interact with PC2. CT **peptide** inhibition could not be competitively blocked by preincubation with truncated CT **peptide** forms, supporting an absolute requirement for the Lys-Lys pair in initial binding of the CT **peptide** to the active site.

L4 ANSWER 7 OF 115 MEDLINE DUPLICATE 3
AN 2001132004 MEDLINE
DN 20565873 PubMed ID: 11113331
TI Prosaptide exacerbates ischemia-induced behavioral deficits in vivo; an effect that does not involve mitogen-activated protein kinase activation.
AU Lapchak P A; Araujo D M; Shackelford D A; Zivin J A
CS University of California San Diego, Department of Neuroscience, MTF 316, 9500 Gilman Drive, La Jolla CA 92093-0624, USA.. plapchak@ucsd.edu
NC NS23814 (NINDS)
NS28121 (NINDS)
SO NEUROSCIENCE, **(2000)** 101 (4) 811-4.
Journal code: 7605074. ISSN: 0306-4522.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301
AB Prosaposin is a 517 amino acid membrane component and secreted protein(5,7,9) that is proteolytically cleaved to generate the four small glycoproteins; saposins A, B, C and D.(9,13,19) Prosaposin's ability to promote neurite outgrowth(31) and to protect neurons from programmed cell death(28) in vitro, as well as to rescue neurons from ischemia and other damage in vivo(11,12,15,25) implied that prosaposin was neurotrophic/neuroprotectant.(1,7,24,31) The neurotrophic sequence of prosaposin was isolated to smaller **peptide** fragments termed prosaptides(15,31) within the amino terminal portion of saposin C.(1,6,8,10,17,20,21,28) The proposed use of synthetic prosaptides as peripherally administered neuroprotective and/or neurotrophic therapeutic agents has stemmed from their ability to cross the blood-brain barrier,(27) as well as their reported neurotrophic activity in vitro.(15,23,31) Few studies, however, have attempted to characterize these **peptides**, presumably due to their reported instability following peripheral administration.(27) With the recent design of a stable 11-mer **retro-inverso** prosaptide,(15,31) it has become feasible to investigate the pharmacological effects of a stable version of these **peptides** in the validated rabbit spinal cord ischemia model that has been used extensively in the development of therapeutics to treat ischemic stroke.(4,14,16,18) Our results show not only that prosaptide was not neurotrophic/neuroprotectant in vivo, but rather it worsened ischemia-induced behavioral deficits.

L4 ANSWER 8 OF 115 MEDLINE DUPLICATE 4
AN 2000493919 MEDLINE
DN 20344114 PubMed ID: 10888201
TI Synthesis and anti-aggregatory activity of linear **retro-inverso** RGD **peptides**.
AU Dal Pozzo A; Fagnoni M; Bergonzi R; Vanini L; de Castiglione R; Aglio C; Colli S
CS G. Ronzoni Institute of Chemical and Biochemical Research, Milan, Italy.. dalpozzo@ronzoni.it
SO JOURNAL OF PEPTIDE RESEARCH, **(2000 Jun)** 55 (6) 447-54.

Journal code: 9707067. ISSN: 1397-002X.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001019
AB Six **retro-inverso** tri- and tetrapeptide analogues of RGD were prepared and their anti-aggregatory activity was determined by platelet aggregation tests in comparison with the corresponding parent **peptides**. An efficient method for the introduction of a malonyl-aspartic residue into a **peptide** chain is described for the first time. A 2-3-fold decrease in potency or total loss of bioactivity was observed with the new **peptides**; structure-activity relationships are discussed.

L4 ANSWER 9 OF 115 MEDLINE DUPLICATE 5
AN 2001021901 MEDLINE
DN 20449182 PubMed ID: 10991978
TI **Retro-inverso** prosaptide **peptides** retain bioactivity, are stable In vivo, and are blood-brain barrier permeable.
AU Taylor E M; Otero D A; Banks W A; O'Brien J S
CS Department of Neurosciences, University of California, San Diego, La Jolla, California, USA.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, **(2000 Oct)** 295 (1) 190-4.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001103
AB Prosaptide (trademark of Myelos Corporation, San Diego, CA) **peptides** are based on the 14-amino-acid neurotrophic sequence of human prosaposin and, like the parent protein, have potent neurotrophic and neuroprotective properties. We previously examined the in vivo stability of a series of bioactive Prosaptide **peptides** and designed **peptides** with increased enzymatic stability in the central and peripheral nervous systems. In this article, we examined the stability, biological activity, and permeability of the blood-brain barrier to **retro-inverso** Prosaptide peptidomimetics. Retro-inversion both reverses the primary sequence and replaces L-amino acids with D-amino acids. We examined the bioactivity of five peptidomimetics, Prosaptides D1-D5. Prosaptide D1, a **peptide** containing all D-amino acids with the primary sequence intact, was inactive. However, four **retro-inverso** peptidomimetics, Prosaptides D2-D5 retained bioactivity in neurite outgrowth and [(35)S]GTPgammaS binding assays. We focused on Prosaptide D4 as a prototypical **retro-inverso** Prosaptide peptidomimetic for further study. (125)I-Prosaptide D4 remained intact in brain or serum for 60 min after i.v. administration and was transported across the blood-brain barrier with a unidirectional influx constant of 2.5 x 10(-4) ml. g(-1). min(-1). We conclude that **retro-inverso** Prosaptide peptidomimetics are excellent candidates for development as therapeutics for central nervous system neurodegeneration.

L4 ANSWER 10 OF 115 MEDLINE DUPLICATE 6
AN 2000092439 MEDLINE
DN 20092439 PubMed ID: 10628817

TI A **retro-inverso** miniantibody with anti-HIV activity.
AU Levi M; Hinkula J; Wahren B
CS Department of Virology, Swedish Institute for Infectious Disease Control and Karolinska Institute, Solna.. michael.levi@smi.ki.se
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, **(2000 Jan 1)** 16 (1) 59-65. Journal code: 8709376. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 200002
ED Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000215
AB An HIV-1-specific miniantibody, a **peptide** representing the third heavy chain complementarity-determining region (CDR) of an HIV-specific mouse antibody, was characterized and modified with unnatural D-isomeric amino acids. The CDR **peptide** and its parent antibody bound to a similar epitope, located in the V3 region of HIV-1 gp120. A shortened CDR sequence was modified with D-amino acids to create an all-D-amino acid **retro-inverso** (RI) **peptide** with a reversed sequence order. The RI CDR was less susceptible to proteolytic degradation than its L-counterpart and had a higher affinity for HIV-1 **peptides**. The miniantibody and its parent antibody showed neutralization of both primary and laboratory strains of HIV-1. In accordance with the binding studies, the RI CDR showed a stronger HIV-inhibiting capacity than its L-counterpart. We conclude that the anti-HIV **retro-inverso** CDR identified in this study has the potential to become a future anti-HIV drug. It has a virus-neutralizing capacity in vitro and appears to be stable. Future research should focus on characterizing its antiviral activity in vivo.

L4 ANSWER 11 OF 115 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:89836 BIOSIS
DN PREV200100089836
TI Dopaminergic neurons rescued from death by ProsaptideTm D5 in MPTP-treated mice.
AU Liu, J. (1); O'Brien, J. S.
CS (1) UCSD Sch Med, La Jolla, CA USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-381.24. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English
AB ProsaptideTM D5 is a **retro-inverso** 11-mer **peptide** derived from the neurotrophic sequence of Prosaposin in the saposin C domain. D5 is stable to protease breakdown and crosses the blood-brain barrier intact. We presented in vitro data earlier (639.2, 29th Neuroscience Meeting, 1999, Miami) that D5 rescued DA neurons from MPP+-mediated toxicity; D5 supported cell survival and potentiated neurite sprouting in primary DA cultures. In this abstract, D5 rescued DA neurons from death in vivo in MPTP-treated C57BL/6 mice. After 24 h treatment with MPTP (40 mg/kg, i.p.), D5 was injected i.p. 3 times per week for 2 weeks. MPTP treatment decreased the number of DA neurons in the substantia nigra (SN) to 30% of controls ($P<0.0001$ vs controls). The effect of D5 treatment was dose-dependent in rescuing DA neurons from death; a dose of 50mg/kg increased the number of surviving DA neurons to 63% of controls; a high dose of 200mg/kg rescued DA neurons to 93% of control values ($P>0.05$ vs controls). A scrambled **peptide** was ineffective at 200mg/kg. ProsaptideTM D5 appears to be a useful agent in the rescue of DA neurons and may have therapeutic potential for the therapy of Parkinson's disease.

(Work supported in part by a grant from Myelos Neurosciences to JSO.)

L4 ANSWER 12 OF 115 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:78061 BIOSIS
DN PREV200100078061
TI A stable prosaposin **retro-inverso peptide** exacerbates ischemia-induced behavioral deficits in rabbits: comparison with the neuroprotective neurosteroid dehydroepiandrosterone sulfate.
AU Chapman, D. F. (1); Araujo, D. M.; Zivin, J. A.; Lapchak, P. A.
CS (1) UCSD, La Jolla, CA USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-287.5. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English
AB Evidence suggests that prosaposin and neurosteroids can rescue neurons from ischemic damage and excitoxicity. Because of their potential neuroprotective properties, both RIP and DHEAS may be useful in treating ischemic stroke. We examined the behavioral effects of a stable 11-mer RIP also known as Prosaptide (all D amino acids: LLEETANNDLL) and DHEAS in rabbits exposed to reversible spinal cord ischemia produced by temporary occlusion of the infrarenal aorta; RIP (1 mg/kg) or DHEAS (50 mg/kg) were administered IV 5 minutes following various durations of aortic occlusion ranging from 15 to 60 min, which allows for the calculation of the duration (min) associated with a 50% probability of permanent paraplegia (P50) for each experimental group. A drug was considered to be neuroprotective only if it prolonged the P50 compared to the vehicle-treated control group, which was approximately 25-28 min. Treatment with RIP significantly ($p<0.05$) decreased the P50 to 20 min (20% reduction), whereas DHEAS significantly ($p<0.05$) prolonged the P50 to 38 min (35% increase). The prominent neuroprotective effects that were observed with DHEAS included increased mobility, tactile sensation and hind limb use. In contrast, RIP exacerbated ischemia-induced behavioral deficits and increased paraplegia. Overall, our study shows that although neurotrophic-like properties have been documented for both RIP and DHEAS, only the latter promotes recovery of spinal cord neuron function following ischemia, suggesting that it may have therapeutic benefits for the treatment of ischemic stroke.

L4 ANSWER 13 OF 115 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:292029 BIOSIS
DN PREV200000292029
TI Modulators of beta-amyloid **peptide** aggregation comprising D-amino acids.
AU Findeis, Mark A. (1); Gefter, Malcolm L.; Musso, Gary; Signer, Ethan R.; Wakefield, James; Molineaux, Susan; Chin, Joseph; Lee, Jung-J; Kelley, Michael; Komar-Panicucci, Sonj; Arico-Muendel, Christopher C.; Phillips, Kathryn; Hayward, Neil J.
CS (1) North Grafton, MA USA
ASSIGNEE: Praecis Pharmaceuticals, Inc., Cambridge, MA, USA
PI US 5985242 November 16, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents, (**Nov. 16, 1999**) Vol. 1228, No. 3, pp. No pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB Compounds that modulate natural beta amyloid **peptide** aggregation are provided. The modulators of the invention comprise a **peptide**, preferably based on a beta amyloid **peptide**, that is comprised entirely of D-amino acids. Preferably, the **peptide** comprises 3-5 D-amino acid residues and includes at least two D-amino acid residues

independently selected from the group consisting of D-leucine, D-phenylalanine and D-valine. In a particularly preferred embodiment, the **peptide** is a **retro-inverso** isomer of a beta amyloid **peptide**, preferably a **retro-inverso** isomer of Abeta17-21. In certain embodiments, the **peptide** is modified at the amino-terminus, the carboxy-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxy-terminal modifying groups include an amide group, an alkyl amide group, an aryl amide group or a hydroxy group. Pharmaceutical compositions comprising the compounds of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compounds of the invention, are also disclosed.

L4 ANSWER 14 OF 115 MEDLINE DUPLICATE 7
AN 1999121111 MEDLINE
DN 99121111 PubMed ID: 9920919
TI Solution structure of a **retro-inverso peptide** analogue mimicking the foot-and-mouth disease virus major antigenic site. Structural basis for its antigenic cross-reactivity with the parent **peptide**.
AU Petit M C; Benkirane N; Guichard G; Du A P; Marraud M; Cung M T; Briand J P; Muller S
CS Laboratoire de Chimie-Physique Macromoleculaire, UMR 7568 CNRS, ENSIC-INPL, 54000 Nancy, France.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1999 Feb 5)** 274 (6) 3686-92. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1BCV; PDB-1BFW
EM 199902
ED Entered STN: 19990316
Last Updated on STN: 20000303
Entered Medline: 19990226
AB The antigenic activity of a 19-mer **peptide** corresponding to the major antigenic region of foot-and-mouth disease virus and its retro-enantiomeric analogue was found to be completely abolished when they were tested in a biosensor system in trifluoroethanol. This suggests that the folding pattern, which is alpha-helix in trifluoroethanol (confirmed by CD measurement), does not correspond to the biologically relevant conformation(s) recognized by antibodies. The NMR structures of both **peptides** were thus determined in aqueous solution. These studies showed that the two **peptides** exhibit similar folding features, particularly in their C termini. This may explain in part the cross-reactive properties of the two **peptides** in aqueous solution. However, the **retro-inverso** analogue appears to be more rigid than the parent **peptide** and contains five atypical beta-turns. This feature may explain why **retro-inverso** foot-and-mouth disease virus **peptides** are often better recognized than the parent **peptide** by anti-virion antibodies.

L4 ANSWER 15 OF 115 MEDLINE DUPLICATE 8
AN 1999388009 MEDLINE
DN 99388009 PubMed ID: 10458771
TI Inhibition of experimental autoimmune encephalomyelitis in SJL mice by oral administration of **retro-inverso** derivative of encephalitogenic epitope P87-99.
AU Marino M; Ippolito A; Fassina G
CS Biopharmaceuticals, TECNOGEN S.C.p.A., Science Park, Piana di Monte Verna, Italy.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1999 Aug)** 29 (8) 2560-6. Journal code: 1273201. ISSN: 0014-2980.

CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990914
AB **Retro-inverso** modification of **peptides** preserves parent **peptide** overall topology and provides at the same time stability to proteolysis, leading to derivatives with prolonged half-life in vitro and in vivo. In this study the encephalitogenic epitope P87 - 99 of myelin basic protein has been prepared in the **retro-inverso** form to examine its biological activity in a murine model of multiple sclerosis. Experiments of in vivo T cell tolerance induction in SJL mice revealed that the **retro-inverso peptide** was able to induce a selective T cell hyporesponsiveness, as measured by a reduction in the proliferative response of lymphnode T cells after antigen challenge. Oral administration of **retro-inverso peptide** decreased the disease severity significantly and delayed considerably the disease onset in treated mice. Enhancement of resistance to proteolysis by **retro-inverso** modification of encephalitogenic epitopes may increase the therapeutic value of oral tolerance induction in the treatment of multiple sclerosis and other Th1-associated inflammatory disorders.

L4 ANSWER 16 OF 115 MEDLINE DUPLICATE 9
AN 1999447490 MEDLINE
DN 99447490 PubMed ID: 10516644
TI Novel strategies for the design of receptor-selective vasopressin analogues: Aib-substitution and **retro-inverso** transformation.
AU Howl J; Prochazka Z; Wheatley M; Slaninova J
CS Molecular Pharmacology Group, School of Health Sciences, University of Wolverhampton, Wolverhampton WV1 1DJ, UK.
SO BRITISH JOURNAL OF PHARMACOLOGY, **(1999 Oct)** 128 (3) 647-52.
Journal code: 7502536. ISSN: 0007-1188.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991222
AB 1. We determined the pharmacological profile of novel backbone-modified **peptides** designed as protease-resistant, selective analogues of AVP. Binding affinities of **peptides** were determined at both V1A and V2 subtypes of vasopressin receptor (VPR). Biological potencies of selected **peptides** were tested in pressor and antidiuretic bioassays. 2. Substitution of the achiral alpha-aminoisobutyric acid (Aib) at position 4 or 7 of AVP produced **peptides** that selectively bound the V2 VPR. Both [Aib4]AVP (140 IU mg-1) and [Aib7]AVP (36 IU mg-1) are selective antidiuretic agonists with little or no activity in uterotonic and pressor assays. 3. [Aib4] and [Aib7] derivatives of the linear V1A-selective antagonist [PhaaDTyr(Et)2Arg6Tyr(NH2)9]AVP bound selectively and with high affinity (Kd 0.51 and 4.1 nM respectively) to the V1A VPR. Bioassays confirmed that these **peptides** were potent antivasopressor agents (pA2 8.10 and 8.36 respectively). 4. A total **retro-inverso** strategy was used to prepare protease-resistant mimetics of both AVP and linear V1A-selective antagonists. Cyclic **retro-inverso** mimetics of AVP did not bind either V1A or V2 VPRs. In contrast,

rationally designed **retro-inverso** mimetics of linear V1A-selective antagonists selectively bound the V1A VPR. 5. Our findings indicate novel methods to improve the pharmacodynamic and pharmacokinetic parameters of neurohypophysial hormone analogues which could be equally applicable to other **peptide**-receptor systems.

L4 ANSWER 17 OF 115 MEDLINE
AN 1999258094 MEDLINE
DN 99258094 PubMed ID: 10326244
TI Observations on the origin of the non-linear van't Hoff behaviour of polypeptides in hydrophobic environments.
AU Boysen R I; Wang Y; Keah H H; Hearn M T
CS Department of Biochemistry and Molecular Biology, Monash University, Clayton, Victoria, Australia.
SO BIOPHYSICAL CHEMISTRY, **(1999 Mar 29)** 77 (2-3) 79-97.
Journal code: 0403171. ISSN: 0301-4622.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990526
AB In this paper we describe a general procedure to determine the thermodynamic parameters associated with the interaction of polypeptides or proteins with immobilised lipophilic compounds such as non-polar n-octyl groups. To this end, the binding behaviour of an all L-alpha-polypeptide, 1, and its **retro-inverso**-isomer, 2, has been investigated with an n-octylsilica and water-organic solvent mixture containing different percentages of acetonitrile or methanol over the temperature range of 278-338 K. The results confirm that non-linear van'ts Hoff plots occur with this pair of polypeptide isomers, depending on the solvent composition. These findings are consistent with the changes in the thermodynamic parameters, enthalpy of association, delta Hoassoc,i, entropy of association, delta Soassoc,i, and heat capacity, delta Cop,i, all having significant temperature dependencies. Theoretical relationship linking the changes in the delta Hoassoc,i, delta Soassoc,i and delta Cop,i values of these polypeptide-non-polar ligate systems, as a function of temperature, T, have been validated. Significant differences were observed in the magnitudes of these thermodynamic quantities when acetonitrile or methanol was employed as the organic solvent. The origin of these solvent-dependent effects can be attributed to the hydrogen-bonding propensity of the respective solvent. Involvement of enthalpy-entropy compensation effects associated with the interaction of these polypeptides with the hydrophobic ligates has also been documented. Analysis of empirical extra-thermodynamic relationships associated with molecular structural properties of these polypeptides, such as the slope term, S, derived from the plots of the logarithmic capacity factor, log k'i, of these polypeptides vs. the volume fraction of the organic solvent, [symbol: see text] as a function of temperature, T, has also revealed similar correlations in terms of the interactive behaviour of polypeptides 1 and 2 under these experimental conditions. These findings provide an extended thermodynamic and extra-thermodynamic framework to examine the solvational, conformational and other equilibrium processes that polypeptides (or proteins) can undergo in the presence of n-alkylsilicas or other classes of immobilised hydrophobic surfaces. The experimental approach utilised in this study with these topologically similar polypeptides thus represents a generic procedure to explore the behaviour of polypeptides or proteins in non-polar environments in terms of their molecular properties and the associated linear free energy relationships that determine their interactive behaviour.

L4 ANSWER 18 OF 115 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:281588 BIOSIS
DN PREV199800281588
TI The potential of **retro-inverso peptides** as synthetic vaccines.
AU Van Regenmortel, M. H. V. (1); Guichard, G.; Benkirane, N.; Briand, J.-P.; Muller, S.; Brown, F.
CS (1) Inst. Biol. Mol. et Cell., CNRS UPR 9021, 15 rue Rene Descartes, F-67084 Strasbourg Cedex France
SO Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 139-143. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens. Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization
. ISSN: 0301-5149. ISBN: 3-8055-6640-9.
DT Book; Conference
LA English

L4 ANSWER 19 OF 115 MEDLINE DUPLICATE 10
AN 1998451584 MEDLINE
DN 98451584 PubMed ID: 9776752
TI A **peptide** nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a **retro-inverso** delivery **peptide**. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons.
AU Aldrian-Herrada G; Desarmenien M G; Orcel H; Boissin-Agasse L; Mery J; Brugidou J; Rabie A
CS CNRS-UPR 9055, Biologie des Neurones Endocrines, CCIPE, 141 rue de la Cardonille, 34094 Montpellier Cedex 5, France.
SO NUCLEIC ACIDS RESEARCH, **(1998 Nov 1)** 26 (21) 4910-6.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981223
AB A **peptide** nucleic acid (PNA) antisense for the AUG translation initiation region of prepro-oxytocin mRNA was synthesized and coupled to a r etro-inverso **peptide** that is rapidly taken up by cells. This bioconjugate was internalized by cultured cerebral cortex neurons within minutes, according to the specific property of the vector **peptide** . The PNA alone also entered the cells, but more slowly. Cell viability was unaffected when the PNA concentrations were lower than 10 microM and incubation times less than for 24 h. Magnocellular neurons from the hypothalamic supraoptic nucleus, which produce oxytocin and vasopressin, were cultured in chemically defined medium. Both PNA and vector **peptide**-PNA depressed the amounts of the mRNA coding for prepro-oxytocin in these neurons. A scrambled PNA had no effect and the very cognate prepro-vasopressin mRNA was not affected. The antisense PNA also depressed the immunocytochemical signal for prepro-oxytocin in this culture in a dose- and time-dependent manner. These results show that PNAs driven by the **retro-inverso** vector **peptide** are powerful antisense reagents for use on cells in culture.

L4 ANSWER 20 OF 115 MEDLINE
AN 1999097766 MEDLINE
DN 99097766 PubMed ID: 9881091
TI A '**retro-inverso**' PNA: structural implications for DNA and RNA binding.

AU Krotz A H; Larsen S; Buchardt O; Eriksson M; Nielsen P E
CS Center for Biomolecular Recognition, H. C. Orsted Institute, University of Copenhagen, Denmark.
SO BIOORGANIC AND MEDICINAL CHEMISTRY, **(1998 Nov)** 6 (11) 1983-92.
Journal code: 9413298. ISSN: 0968-0896.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990202
AB **'Retro-inverso' peptide** nucleic acid (PNA) monomers of thymine (T*: N-(amidomethyl)-N-(N1-thyminyl-acetyl)-beta-alanyl) (and adenine) have been prepared and introduced in PNA oligomers. A homo '**retro-inverso**' T*8 PNA was found not to hybridize to a complementary DNA or RNA oligonucleotide, whereas introduction of one **retro-inverso** thymine unit into the middle of a normal PNA 15-mer resulted in a c.a. 8 degrees C destabilization of the complex of this oligomer with a complementary DNA or RNA oligomer. In an effort to compensate for the structural nucleobase 'phase-shift' caused by the T* monomer by also introducing a beta-alanine monomer it is concluded that the effect of the T* backbone is -7 degrees C when hybridizing to DNA and -4.5 degrees C when hybridizing to RNA. Nonetheless, the T* unit shows good sequence discrimination comparable to that of normal PNA. Molecular dynamics simulations indicate an unfavourable conformation of the backbone amide carbonyl group resulting in reduced interaction with the aqueous medium and an 'electrostatic clash' with the carbonyl of the nucleobase linker. These results show that a simple inversion of an amide bond in the PNA backbone has a dramatic, and hardly predictable, effect on the DNA mimicking properties of the oligomer.

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FULL ESTIMATED COST	19.88	20.09

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WEST Search History

DATE: Saturday, June 28, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L3	L2 same eigenvector	1	L3
L2	retro inverso peptide	155	L2
L1	retro inverso same peptide	415	L1

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☐ 1. Document ID: US 20020009756 A1

L3: Entry 1 of 1 File: PGPB Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009756
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020009756 A1

TITLE: Algorithmic design of peptides for binding and/or modulation of the functions of receptors and/or other proteins

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Mandell, Arnold J.	Asheville	NC	US	
Selz, Karen A.	Asheville	NC	US	
Shlesinger, Michael F.	Rockville	MD	US	

US-CL-CURRENT: 435/7.2; 530/333, 702/19

ABSTRACT:

Methods of designing protein-targeted peptides or peptide analogues whose sequences are derived from the target protein sequences, using target protein sequence, analytically derived templates, and relevant distributions of amino acids for weighted random assignments to those templates. The templates are derived from eigenvectors of the autocovariance matrices of the physicochemically-transformed amino acid sequence of the target proteins; wavelet subsequence templates derived from wavelet transformations of the physicochemically-transformed amino acid sequence of the target proteins; and/or non-overlapping redundant subsequence templates computed from the physicochemically-transformed target protein amino acid sequence. The protein targets include cell receptors; transporters; enzymes; chaperonins; antibodies; surface proteins of infectious agents; and any protein involved in protein-protein interactions. The peptides are designed to bind to and/or otherwise modulate the function of the target protein. Partitioned amino acid distributions for weighted random assignments to the similarly partitioned templates are derived from a variety of physiologically relevant amino acid pools or regions in the target protein sequence relevant to the construction of the templates. Sequential pattern ("mode") matches between candidate peptides and their target proteins are designed such that when examined by maximum entropy, all poles power spectral transformations and/or wavelet transformations, they yield peaks of wavenumbers that differ by .ltoreq.10% of the larger wavenumber value. Also provided are examples of such mode-matched peptides, as well as methods for their use in elucidating sites on proteins for drug design and testing, detection of disease conditions or contaminants, and as therapeutics for protein function modulation in disease treatment.

L3: Entry 1 of 1 File: PGPB Jan 24, 2002

DOCUMENT-IDENTIFIER: US 20020009756 A1
TITLE: Algorithmic design of peptides for binding and/or modulation of the functions of receptors and/or other proteins

CLAIMS:

1. A method for synthesizing a peptide based on matching a physicochemical mode of a peptide to the same physicochemical mode of a target polypeptide or protein, followed by synthesizing a retro-inverso peptide version of said peptide comprised of D-amino acids, comprising the steps of: assigning a numerical value of an orderable physicochemical property to each member of a set of peptide constituents, said set of peptide constituents including all the members of the set of naturally-occurring L-amino acids; arranging said peptide constituents in order of said numerical values of said orderable physicochemical property; partitioning said set of peptide constituents into a plurality of peptide constituent groups, whereby each of said peptide constituent groups contains at least one member of said set of peptide constituents, each peptide constituent group encompasses a range of said ordered numerical values, and each member of said set of peptide constituents belongs to only one peptide constitutent group; creating a polypeptide physicochemical data series by replacing each amino acid in an amino acid sequence of said target polypeptide or protein with said numerical value of said orderable physicochemical property corresponding to said each amino acid in said amino acid sequence of said target polypeptide or protein; calculating one or more polypeptide eigenvalues and a corresponding polypeptide eigenvector associated with each of said one or more polypeptide eigenvalues by linear decomposition of an autocovariance matrix formed from a sequentially lagged data matrix of said polypeptide physicochemical data series; ordering said one or more polypeptide eigenvalues and said corresponding polypeptide eigenvectors from largest to smallest; selecting one or more of said polypeptide eigenvectors; transforming said one or more of said polypeptide eigenvectors into an eigenvector template; forming a graph of said eigenvector template, wherein said numerical values of said physicochemical property are graphed along the y-axis of said graph and ordered position in said eigenvector template is graphed along the x-axis of said graph; partitioning said graph along said y-axis according to said ranges of said numerical values of said physicochemical property defining said peptide constituent groups, to form a plurality of y-axis ranges; assigning one of said peptide constituents to each position in said peptide by using said graph as a template to create a sequence of a mode-matched peptide, wherein at each ordered position in said eigenvector template along said x-axis of said graph, said one of said peptide constituents assigned to said ordered position has a value of said orderable physicochemical property that is within said y-axis range of said ordered point; determining a sequence of a retro-inverso peptide by inverting said sequence of a mode-matched peptide; and synthesizing said retro-inverso peptide from said sequence, using D-amino acids.

2. A method for synthesizing a peptide based on matching a physicochemical mode of a peptide to the same physicochemical mode of a target polypeptide or protein, followed by synthesizing a retro-inverso version of said peptide comprised of D-amino acids, comprising the steps of: assigning a numerical value of an orderable physicochemical property to each member of a set of peptide constituents, said set of peptide constituents including all the members of the set of naturally-occurring amino acids; arranging said peptide constituents in order of said numerical values of said orderable physicochemical property; partitioning said set of peptide constituents into a plurality of peptide constituent groups, whereby each of said peptide constituent groups contains at least one member of said set of peptide constituents, each peptide constituent group encompasses a range of said ordered numerical values, and each member of said set of peptide constituents belongs to only one peptide constituent group; creating a polypeptide physicochemical data series by replacing each amino acid in an amino acid sequence with said numerical value of said orderable physicochemical property corresponding to said each amino acid in said amino acid sequence; calculating one or more polypeptide eigenvalues and a corresponding polypeptide eigenvector associated with each of said one or more polypeptide eigenvalues by linear decomposition of an autocovariance matrix formed from a sequentially lagged data matrix of said polypeptide physicochemical data series; ordering said one or more polypeptide eigenvalues and said corresponding polypeptide eigenvectors from largest to smallest; selecting one or more of said polypeptide eigenvectors; forming a vector, said vector being a sum of the products of each of said plurality of said polypeptide eigenvectors multiplied by the

corresponding eigenvalue; forming a graph of said vector, wherein said numerical values of said orderable physicochemical property are graphed along the y-axis of said graph, and ordered position in said eigenvector template is graphed along the x-axis of said graph; partitioning said graph along said y-axis according to said range of said numerical values of said orderable physicochemical property defining said peptide constituent groups, to form a plurality of y-axis ranges; and assigning one of said peptide constituents to each position in said peptide by using said graph of said vector as a template, wherein at each ordered position in said eigenvector template along said x-axis of said graph, said one of said peptide constituents assigned to said ordered position has a value of said orderable physicochemical property that is within said y-axis range of said ordered position; determining a sequence of a retro-inverso peptide by inverting said sequence of a mode-matched peptide; and synthesizing said retro-inverso peptide from said sequence, using D-amino acids.

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